FDA Urged to Ban Drug Used In Effort to Bar Heart Attacks

By Morton Mintz
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Ten years ago, leaders of the medical research establishment—mainly philanthropist Mary Lasker, then-Sen. Lister Hill (D-Ala.) and famed heart surgeon Michael E. de Bakey—began to lead a chorus of acclaim for the seeming potential of a prescription drug called Atromid-S to prevent heart attacks.

De Bakey appeared before Hill's Senate Appropriations subcommittee to make an impassioned plea for a $49 million government study of the drug. Hill nearly got a $4 million down payment through Congress. Lasker invited reporters to her home to hear a report on Atromid's supposed wondrous promise, and shortly a front-page story, headlined, "Drug Curb Hinted for Heart Attack," appeared in the New York Times.

The effectiveness of Atromid in preventing heart attacks has yet to be established. But a report being published today on a carefully controlled study in men shows a 54 per cent higher incidence of gall bladder disease in Atromid users than in comparable non-users.

On the basis of the report, the Health Research Group (HRG), which is affiliated with Ralph Nader, petitioned the Food and Drug Administration to start proceedings to take Atromid off the market.

An FDA spokesman said the agency will study the report, published in the New England Journal of Medicine. The manufacturer, the Ayerst Laboratories division of American Home Products Corp., did not reply to a reporter's request for comment. Its Atromid sales have been at an annual rate of $30 million.

Dr. Sidney M. Wolfe, director of the HRG, estimated that 1,000 men a year will get gall bladder disease because of Atromid. He calculated the number of current users at 743,000, including 450,000 men, and speculated that the drug may cause the disease in women, too.

Ayerst holds the American patent on Atromid (clofibrate), which was first sold in Britain. The FDA released it to the American market in May, 1967.

In approving it, the agency permitted Ayerst to make no claim that Atromid would prevent heart attacks. Instead, it limited the prescribing instructions, or physician labeling, to what Ayerst's data demonstrated: the drug lowered blood levels of fatty substances known as serum lipids, particularly triglycerides and cholesterol.

Then and now, the labeling emphasized that scientists have not established whether drug-induced lowering of serum lipids has "a detrimental, beneficial, or no effect" on cardiovascular death or disease.

Medical scientists hotly dispute whether decreasing serum lipids is therapeutically beneficial, just as they dispute whether the so-called hypoglycemics, drugs which lower blood sugar, protect against the dread cardiovascular complications of diabetes.

In 1966, what is now the National Heart, Lung, and Blood Institute, a unit of the National Insitutues of Health, started the huge Coronary Drug Project to find out if the risk of a new heart attack in men who already had had one would be lessened by any of the following: Ayerst's Premarin, an estrogen, in either of two doeses; Travenol Laboratories Choxin (sodium dextrothyroxine); niacin (nicotinic acid) or Atromid.

The results were discouraging. The project stopped using Premarin in one dose in 1970 chiefly because it caused an excess of nonfatal heart disease, and the other dose because of an excess of blood clotting and cancer; Choloxin in 1971, because the death rate was higher among users than non-users, and niacin and Atromid in 1974, because neither significantly decreased the death rate below that achieved with a dummy drug, and because of unpleasant and hazardous adverse reactions affecting the digestive and cardiovascular systems.

Dr. Robert S. Gordon Jr., an NIH official, and four colleagues who prepared the New England Journal report disclosed that 4 per cent of 1,051 men on Atromid devcloped gall bladder disease, compared with 2.6 per cent of 2,670 men on a placebo, or fake drug. Gordon said the results apply to all middle-aged men on the drug, not merely to those who have had heart attacks.

The HRG's Wolfe said the report "refocuses attention" on the question of why more than 1 million persons are taking any drugs to lower serum cholesterol.

In 1967 and 1968, without the knowledge or backing of Heart Institute director Donald S. Frederickson, now head of the NIH, philanthropist Lasker and her allies proposed government funding of a separate Atromid study that would have enrolled 16,000 men—twice as many as in the entire Coronary Drug Project.

The proposal originated with Dr. Louis R. Krasno, a United Airlines medical official who said a study he had done in 1,200 middle-aged men indicated that for every heart attack in Atromid users, non-users had 3.7. Supporting him, statistician John W. Weiner told Sen. Hill that Atromid was "free of serious side effects."